CENTER FOR DRUG EVALUATION AND RESEARCH

Approval Package for:

Application Number : 074799

Trade Name : FLUOCINONIDE TOPICAL SOLUTION

Generic Name: Fluocinonide Topical Solution

Sponsor : Taro Pharmaceuticals

Approval Date: December 31, 1996

ANDA 74-799

DEC 31 1996

Taro Pharmaceuticals Inc.
Attention: Avraham Yacobi, Ph.D.
5 Skyline Drive
Hawthorne, NY 10532

Dear Sir:

This is in reference to your abbreviated new drug application dated November 30, 1995, submitted pursuant to Section 505(j) of the Federal Food, Drug, and Cosmetic Act, for Fluocinonide Topical Solution USP, 0.05%.

Reference is also made to your amendments dated October 30, November 27, December 12, and December 18, 1996.

We have completed the review of this abbreviated application and have concluded that the drug is safe and effective for use as recommended in the submitted labeling. Accordingly, the application is approved. The Division of Bioequivalence has determined your Fluocinonide Topical Solution USP, 0.05% to be bioequivalent to the listed drug (Lidex® Topical Solution of Hamilton Pharma Inc.).

Under 21 CFR 314.70, certain changes in the conditions described in this abbreviated application require an approved supplemental application before the change may be made.

Post-marketing reporting requirements for this abbreviated application are set forth in 21 CFR 314.80-81. The Office of Generic Drugs should be advised of any change in the marketing status of this drug.

We request that you submit, in duplicate, any proposed advertising or promotional copy which you intend to use in your initial advertising or promotional campaigns. Please submit all proposed materials in draft or mock-up form, not final print. Submit both copies together with a copy of the proposed or final printed labeling to the Division of Drug Marketing, Advertising, and Communications (HFD-240). Please do not use Form FD-2253 (Transmittal of Advertisements and Promotional Labeling for Drugs for Human Use) for this initial submission.

We call your attention to 21 CFR 314.81(b)(3) which requires that materials for any subsequent advertising or promotional campaign be submitted to our Division of Drug Marketing, Advertising, and Communications (HFD-240) with a completed Form FD-2253 at the time of their initial use.

Sincerely yours,

D. L. Sporn 12/31/96

Douglas L. Sporn
Director
Office of Generic Drugs
Center for Drug Evaluation and Research

CC: ANDA 74-799
ANDA 74-799/Division File
Field Copy
HFD-600/Reading File
HFD-610/J.Phillips
HFD-008/P.Savino
HFD-93

Endorsements:
HFD-613/L.Golson/12-23-96 Gilmore for 12/23/96
HFD-613/J.Grace/12-23-96 C. Halquist for J.Grace 12/23/96
HFD-627/N.Nashed, Ph.D./12-23-96 N.Nashed 12/23/96
HFD-627/P.Schwartz, Ph.D./12-23-96 P.J. 12/23/96
HFD-617/J.Buccine/12-23-96 JB 12/23/96
Drafted: J.Buccine 12-22-96
X:\NEW\FIRMSNZ\TARO\74799.AP
F/T by MM December 23, 1996

APPROVAL LETTER

12/31/96

DO NOT ACCEPT IF SEAL IS BROKEN OR MISSING.
NDC 51672-1273-2

20 mL

Fluocinonide Topical Solution USP, 0.05%

DEC 31 1996

TARO

FOR TOPICAL USE ONLY.
NOT FOR OPHTHALMIC USE.
CAUTION: Federal law prohibits dispensing without prescription.

FORMULA: Fluocinonide 0.5 mg/mL in a solution of alcohol (35%), citric acid, diisopropyl adipate and propylene glycol.
USUAL DOSAGE: A small amount should be applied to the affected area two to four times daily, as needed.
SEE PACKAGE INSERT FOR FULL PRESCRIBING INFORMATION.
STORE AT ROOM TEMPERATURE. AVOID EXCESSIVE HEAT, ABOVE 40°C (104°F).

SEE BOTTOM FOR LOT NUMBER AND EXPIRATION DATE.
Keep this and all medication out of the reach of children.

Mfd. By:
TARO Pharmaceuticals Inc., Bramalea, Ontario, Canada L6T 1C3

Dist. By:
Taro Pharmaceuticals U.S.A., Inc., Hawthorne, NY 10532

PK 1942-0

Made in Canada.

DO NOT ACCEPT IF SEAL IS BROKEN OR MISSING.
NDC 51672-1273-4

60 mL

Fluocinonide Topical Solution USP, 0.05%

DEC 31 1996

TARO

FOR TOPICAL USE ONLY.
NOT FOR OPHTHALMIC USE.
CAUTION: Federal law prohibits dispensing without prescription.

FORMULA: Fluocinonide 0.5 mg/mL in a solution of alcohol (35%), citric acid, diisopropyl adipate and propylene glycol.
USUAL DOSAGE: A small amount should be applied to the affected area two to four times daily, as needed.
SEE PACKAGE INSERT FOR FULL PRESCRIBING INFORMATION.
STORE AT ROOM TEMPERATURE. AVOID EXCESSIVE HEAT, ABOVE 40°C (104°F).

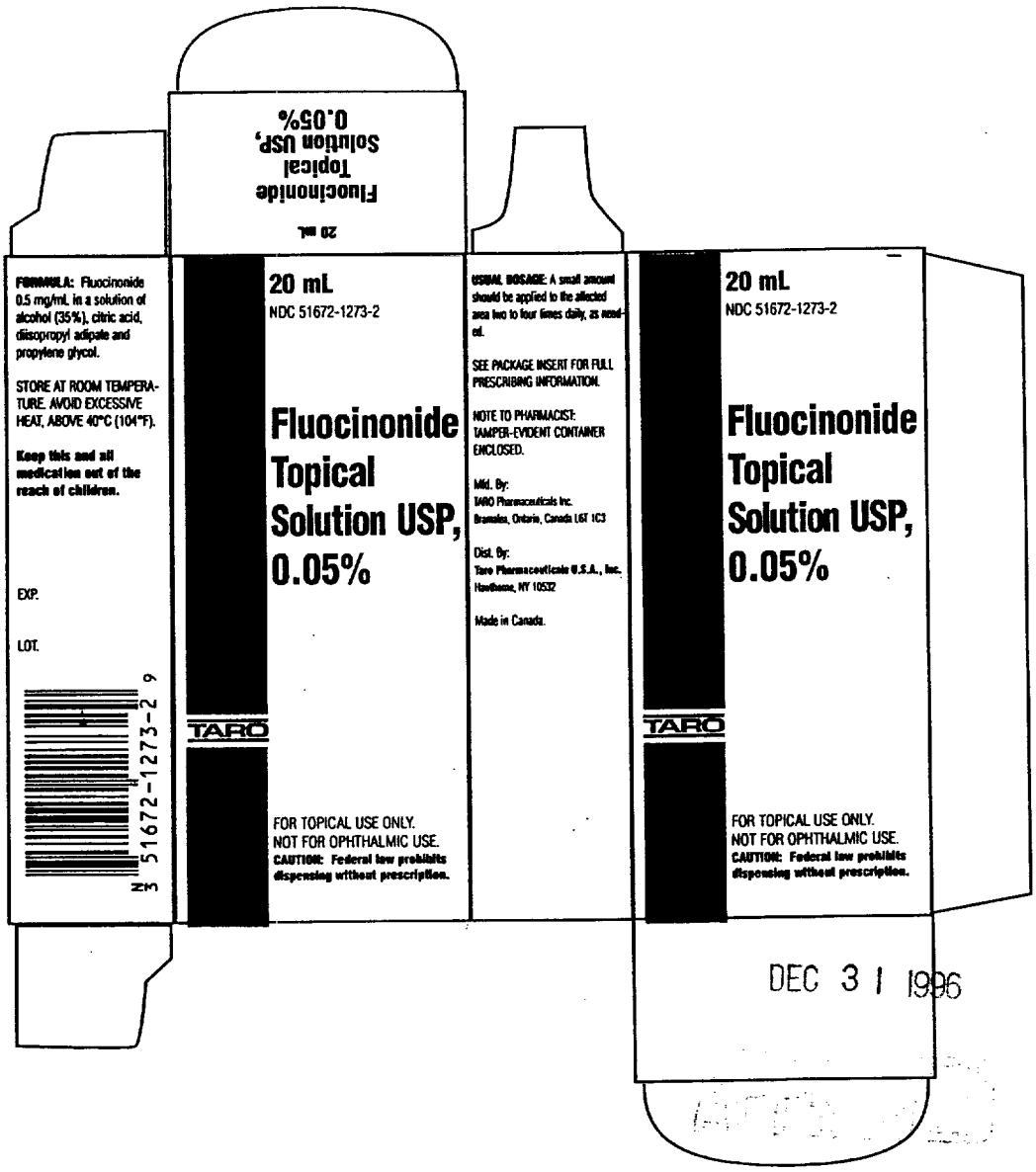
SEE BOTTOM FOR LOT NUMBER AND EXPIRATION DATE.
Keep this and all medication out of the reach of children.

Mfd. By:
TARO Pharmaceuticals Inc., Bramalea, Ontario, Canada L6T 1C3

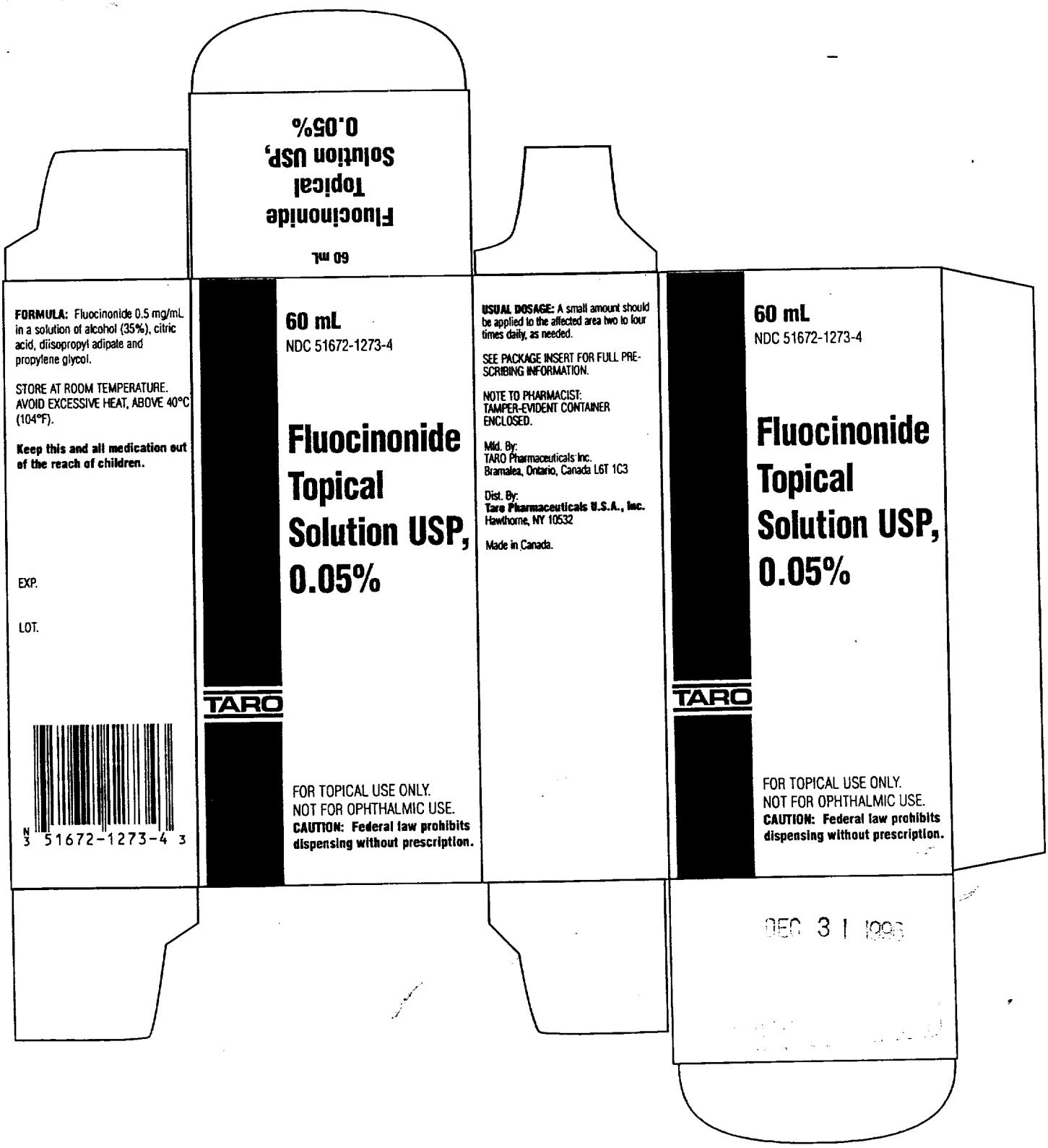
Dist. By:
Taro Pharmaceuticals U.S.A., Inc., Hawthorne, NY 10532

PK 1944-0

Made in Canada.


20 mL
Fluocinonide
Topical
Solution USP,
0.05%
FORMULA: Fluocinonide 0.5 mg/mL in a solution of alcohol (35%), citric acid, diisopropyl adipate and propylene glycol.
STORE AT ROOM TEMPERATURE. AVOID EXCESSIVE HEAT, ABOVE 40°C (104°F).
Keep this and all medication out of the reach of children.
EXP.
LOT.
N 51672-1273-2 9
20 mL
NDC 51672-1273-2
Fluocinonide
Topical
Solution USP,
0.05%
TARO
FOR TOPICAL USE ONLY.
NOT FOR OPHTHALMIC USE.
CAUTION: Federal law prohibits dispensing without prescription.
USUAL DOSAGE: A small amount should be applied to the affected area two to four times daily, as needed.
SEE PACKAGE INSERT FOR FULL PRESCRIBING INFORMATION.
NOTE TO PHARMACIST:
TAMPER-EVIDENT CONTAINER ENCLOSED.
Mfd. By:
TARO Pharmaceuticals Inc.
Brampton, Ontario, Canada L6T 1C3
Dist. By:
Taro Pharmaceuticals U.S.A., Inc.
Hawthorne, NY 10532
Made in Canada.
20 mL
NDC 51672-1273-2
Fluocinonide
Topical
Solution USP,
0.05%
TARO
FOR TOPICAL USE ONLY.
NOT FOR OPHTHALMIC USE.
CAUTION: Federal law prohibits dispensing without prescription.
DEC 31 1996

S96

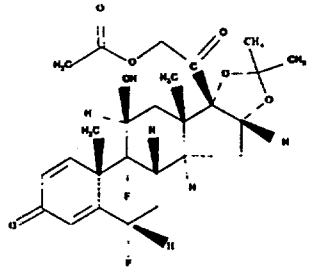

Fluocinonide
Topical
Solution USP,
0.05%
60 mL
FORMULA: Fluocinonide 0.5 mg/mL in a solution of alcohol (35%), citric acid, diisopropyl adipate and propylene glycol.
STORE AT ROOM TEMPERATURE. AVOID EXCESSIVE HEAT, ABOVE 40°C (104°F).
Keep this and all medication out of the reach of children.
EXP.
LOT.
N 3 51672-1273-4 3
TARO
60 mL
NDC 51672-1273-4
Fluocinonide Topical Solution USP, 0.05%
FOR TOPICAL USE ONLY.
NOT FOR OPHTHALMIC USE.
CAUTION: Federal law prohibits dispensing without prescription.
USUAL DOSAGE: A small amount should be applied to the affected area two to four times daily, as needed.
SEE PACKAGE INSERT FOR FULL PRESCRIBING INFORMATION.
NOTE TO PHARMACIST: TAMPER-EVIDENT CONTAINER ENCLOSED.
Mfd. By:
TARO Pharmaceuticals Inc.
Bramalea, Ontario, Canada L6T 1C3
Dist. By:
Taro Pharmaceuticals U.S.A., Inc.
Hawthorne, NY 10532
Made in Canada.
60 mL
NDC 51672-1273-4
Fluocinonide Topical Solution USP, 0.05%
TARO
FOR TOPICAL USE ONLY.
NOT FOR OPHTHALMIC USE.
CAUTION: Federal law prohibits dispensing without prescription.
DEC 3 1

FLUOCINONIDE TOPICAL SOLUTION USP, 0.05%

FOR TOPICAL USE ONLY. NOT FOR OPHTHALMIC USE.

DESCRIPTION

Fluocinonide solution 0.05% is intended for topical administration. The active component is the corticosteroid fluocinonide, which is the 21-acetate ester of fluocinolone acetonide and has the chemical name pregna-1,4-diene-3,20-dione,21-(acetyloxy)-6,9-difluoro-11-hydroxy-16,17-[(1-methylethylidene)bis(oxy)]-,(6α, 11β, 16α)-. It has the following chemical structure:



Molecular Weight:
494.54

Molecular Formula:
$C_{26}H_{32}F_2O_7$

Fluocinonide topical solution contains fluocinonide 0.5 mg/mL in a solution of alcohol (35%), citric acid, diisopropyl adipate, and propylene glycol. In this formulation, the active ingredient is totally in solution.

CLINICAL PHARMACOLOGY

Topical corticosteroids share anti-inflammatory, anti-pruritic and vasoconstrictive actions.

The mechanism of anti-inflammatory activity of the topical corticosteroids is unclear. Various laboratory methods, including vasoconstrictor assays, are used to compare and predict potencies and/or clinical efficacies of the topical corticosteroids. There is some evidence to suggest that a recognizable correlation exists between vasoconstrictor potency and therapeutic efficacy in man.

Pharmacokinetics

The extent of percutaneous absorption of topical corticosteroids is determined by many factors including the vehicle, the integrity of the epidermal barrier, and the use of occlusive dressings. A significantly greater amount of fluocinonide is absorbed from the solution than from the cream or gel formulations.

Topical corticosteroids can be absorbed from normal intact skin. Inflammation and/or other disease processes in the skin increase percutaneous absorption. Occlusive dressings substantially increase the percutaneous absorption of topical corticosteroids. Thus, occlusive dressings may be a valuable therapeutic adjunct for treatment of resistant dermatoses. (See DOSAGE AND ADMINISTRATION.)

Once absorbed through the skin, topical corticosteroids are handled through pharmacokinetic pathways similar to systemically administered corticosteroids. Corticosteroids are bound to plasma proteins in varying degrees. Corticosteroids are metabolized primarily in the liver and are then excreted by the kidneys. Some of the topical corticosteroids and their metabolites are also excreted into the bile.

INDICATIONS AND USAGE

Fluocinonide topical solution 0.05% is indicated for the relief of the inflammatory and pruritic manifestations of corticosteroid responsive dermatoses.

CONTRAINDICATIONS

Topical corticosteroids are contraindicated in those patients with a history of hypersensitivity to any of the components of the preparation.

PRECAUTIONS

General

Systemic absorption of topical corticosteroids has produced reversible hypothalamic-pituitary-adrenal (HPA) axis suppression, manifestation of Cushing's syndrome, hyperglycemia, and glucosuria in some patients. Conditions which augment systemic absorption include the application of the more potent steroids, use over large surface areas, prolonged use, the addition of occlusive dressings, and dosage form.

Therefore, patients receiving a large dose of a potent topical steroid applied to a large surface area or under an occlusive dressing should be evaluated periodically for evidence of HPA axis suppression by using the urinary free cortisol and ACTH stimulation tests. If HPA axis suppression is noted, an attempt should be made to withdraw the drug, to reduce the frequency of application, or to substitute a less potent steroid.

Recovery of HPA axis function is generally prompt and complete upon discontinuation of the drug. Infrequently, signs and symptoms of steroid withdrawal may occur, requiring supplemental systemic corticosteroids. Children may absorb proportionally larger amounts of topical corticosteroids and thus be more susceptible to systemic toxicity. (See PRECAUTIONS - Pediatric Use.)

This preparation is not for ophthalmic use. Severe irritation is possible if fluocinonide solution contacts the eye. If that should occur, immediate flushing of the eye with a large volume of water is recommended.

If irritation develops, topical corticosteroids should be discontinued and appropriate therapy instituted.

As with any topical corticosteroid product, prolonged use may produce atrophy of the skin and subcutaneous tissues. When used on intertriginous or flexor areas, or on the face, this may occur even with short-term use.

In the presence of dermatological infections, the use of an appropriate antifungal or antibacterial agent should be instituted. If a favorable response does not occur promptly, the corticosteroid should be discontinued until the infection has been adequately controlled.

Information for the Patient

Patients using topical corticosteroids should receive the following information and instructions:

1. This medication is to be used as directed by the physician. It is for external use only. Avoid contact with the eyes. If there is contact with the eyes and severe irritation occurs, immediately flush with a large volume of water.
2. Patients should be advised not to use this medication for any disorder other than for which it was prescribed.
3. The treated skin area should not be bandaged or otherwise covered or wrapped as to be occlusive unless directed by the physician.
4. Patients should report any signs of local adverse reactions especially under occlusive dressing.
5. Parents of pediatric patients should be advised not to use tightfitting diapers or plastic pants on a child being treated in the diaper area, as these garments may constitute occlusive dressings.

Laboratory Tests
The following tests may be helpful in evaluating HPA axis suppression:
Urinary free cortisol test
ACTH stimulation test

Carcinogenesis, Mutagenesis, and Impairment of Fertility
Long-term animal studies have not been performed to evaluate the carcinogenic potential or the effect on fertility of topical corticosteroids. Studies to determine mutagenicity with prednisolone and hydrocortisone have revealed negative results.

Pregnancy: Teratogenic Effects
Pregnancy Category C
Corticosteroids are generally teratogenic in laboratory animals when administered systemically at relatively low dosage levels. The more potent corticosteroids have been shown to be teratogenic after dermal application in laboratory animals. There are no adequate and well-controlled studies in pregnant women on teratogenic effects from topically applied corticosteroids. Therefore, topical corticosteroids should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus. Drugs of this class should not be used extensively on pregnant patients, in large amounts, or for prolonged periods of time.

Nursing Mothers
It is not known whether topical administration of corticosteroids could result in sufficient systemic absorption to produce detectable quantities in breast milk. Systemically administered corticosteroids are secreted into breast milk in quantities not likely to have a deleterious effect on the infant. Nevertheless, caution should be exercised when topical corticosteroids are administered to a nursing woman.

Pediatric Use
Pediatric patients may demonstrate greater susceptibility to topical corticosteroid-induced HPA axis suppression and Cushing's syndrome than mature patients because of the larger skin surface area to body weight ratio.

Hypothalamic-pituitary-adrenal (HPA) axis suppression, Cushing's syndrome, and intracranial hypertension have been reported in children receiving topical corticosteroids. Manifestations of adrenal suppression in children include linear growth retardation, delayed weight gain, low plasma cortisol levels, and absence of response to ACTH stimulation. Manifestations of intracranial hypertension include bulging fontanelles, headaches, and bilateral papilledema.

Administration of topical corticosteroids to children should be limited to the least amount compatible with an effective therapeutic regimen. Chronic corticosteroid therapy may interfere with the growth and development of children.

ADVERSE REACTIONS
The following local adverse reactions are reported infrequently with topical corticosteroids, but may occur more frequently with the use of occlusive dressings. These reactions are listed in an approximate decreasing order of occurrence.
Burning
Itching
Irritation
Dryness
Folliculitis
Hypertrichosis
Acneiform eruptions
Hypopigmentation
Perioral dermatitis
Allergic contact dermatitis
Maceration of the skin
Secondary infection
Skin atrophy
Striae
Miliaria

OVERDOSAGE
Topically applied corticosteroids can be absorbed in sufficient amounts to produce systemic effects. (See PRECAUTIONS.)

DOSAGE AND ADMINISTRATION
Fluocinonide Topical Solution USP, 0.05% should be applied to the affected area as a thin film from two to four times daily depending on the severity of the condition.

Occlusive dressings may be used for the management of psoriasis or recalcitrant conditions.

If an infection develops, the use of occlusive dressings should be discontinued and appropriate antimicrobial therapy instituted.

HOW SUPPLIED
Fluocinonide Topical Solution USP, 0.05%.
Plastic squeeze bottles of 20 mL and 60 mL.

Store at room temperature. Avoid excessive heat, above 40°C (104°F).

CAUTION: Federal law prohibits dispensing without prescription.

Mfd. By: TARO Pharmaceuticals Inc.,
Bramalea, Ontario, Canada L6T 1C3

PK-1940-0

P/C 908

Issued: October 10, 1996

1. CHEMISTRY REVIEW NO. 2

2. ANDA # 74-799

3. NAME AND ADDRESS OF APPLICANT

Taro Pharmaceuticals Inc.
130 East Drive
Bramalea, Ontario L6T 1C3
Canada

4. LEGAL BASIS FOR SUBMISSION

In the opinion and to the knowledge of the firm, there are no patents that claim the listed drug referred to in this application, Lidex (Fluocinonide) Topical Solution.

The firm certifies that the reference listed drug is not entitled to a period of marketing exclusivity.

5. SUPPLEMENT(s)

N/A

6. PROPRIETARY NAME

N/A

7. NONPROPRIETARY NAME

Fluocinonide

8. SUPPLEMENT(s) PROVIDE(s) FOR:

N/A

9. AMENDMENTS AND OTHER DATES:

Original 11/30/95
Amendment 2/14/96
Amendment 10/30/96
Amendment 11/18/96
Amendment 11/27/96
Amendment 12/12/96

10. PHARMACOLOGICAL CATEGORY

Anti-inflammatory

11. Rx or OTC

Rx

12. RELATED IND/NDA/DMF(s)

13. DOSAGE FORM

Solution

14. POTENCY

0.05%

15. CHEMICAL NAME AND STRUCTURE

Pregna-1,4-diene-3,20-dione,21-(acetyloxy)-6,9-difluoro-11-hydroxy-16,17-[(1-methylethylidene)bis(oxy)]-,

16. RECORDS AND REPORTS

17. COMMENTS

18. CONCLUSIONS AND RECOMMENDATIONS

The application is approvable.

19. REVIEWER: DATE COMPLETED:

Nashed E. Nashed, Ph.D. 12/17/96

Supervisor: Paul Schwartz, Ph.D. 12-17-96

OFFICE OF GENERIC DRUGS
DIVISION OF BIOEQUIVALENCE

ANDA # 74-799 SPONSOR: Taro Pharmaceuticals U.S.A., Inc.
DRUG: Fluocinonide
DOSAGE FORM: Topical Solution
STRENGTHS/(s): 0.05%
TYPE OF STUDY: Single/Multiple Waiver
STUDY SITE: NOT A FIRST GENERIC

STUDY SUMMARY: As per interim guidance for inactive ingredients for topical solution, this test product comes under the category of Q1 same, Q2 diff. ANDA in this category can be accepted for filing with explanation as long as Q2 is not greater than maximum conc. in the IIG; may require *in vivo* BE study. All excipients in topical products are exception excipients (EE). The difference in the conc. of alcohol and di-isopropyl adipate between test and reference products are less than Propylene glycol in the test product is ore than RLD. However, propylene glycol is EE and its conc. is within the IIG potency range. There is no qualitative difference in ingredients between test and reference product. The pH and specific gravity data provided by the firm show no significant differences between the two products. Therefore, waiver of *in vivo* bioequivalence study is granted under 21 CFR 320.22 (b)(3).

DISSOLUTION: Not applicable

PRIMARY REVIEWER: Kuldeep R. Dhariwal, Ph.D, BRANCH: II

INITIAL: KRDhariwal DATE 5/21/96

BRANCH CHIEF: Shriniwas Nerurkar, Ph.D., BRANCH: II

INITIAL: SNerurkar DATE 5/21/96

DIRECTOR
DIVISION OF BIOEQUIVALENCE: Keith Chan, Ph.D

INITIAL: KC DATE 5/22/96

DIRECTOR
OFFICE OF GENERIC DRUGS:

INITIAL: N/A DATE

9.J

ANDA 74-799

Taro Pharmaceuticals U.S.A., Inc.
U.S. Agent for: Taro Pharmaceuticals, Inc.
Attention: Michael Kohlbrenner
6 Skyline Drive
Hawthorne NY 10532

MAY 23 1996

Dear Sir:

Reference is made to your abbreviated new drug application submitted pursuant to Section 505 (j) of the Federal Food, Drug and Cosmetic Act for Fluocinonide Topical Solution USP, 0.05%.

The Division of Bioequivalence has completed its review and has no further questions at this time.

Please note that the bioequivalency comments expressed in this letter are preliminary. The above bioequivalency comments may be revised after review of the entire application, upon consideration of the chemistry, manufacturing and controls, microbiology, labeling or other scientific or regulatory issues. A revised determination may require additional information and/or studies, or may conclude that the proposed formulation is not approvable.

Sincerely yours,

Keith K. Chan, Ph.D.
Director, Division of Bioequivalence
Office of Generic Drugs
Center for Drug Evaluation and Research

D, J

MAY 21 1996

Fluocinonide Topical Solution,USP
0.05%
ANDA # 74-799
Reviewer: Kuldeep R. Dhariwal
File Name : 74799W.296

Taro Pharmaceuticals U.S.A. Inc.
U.S.Agent for: Taro
Pharmaceuticals, Inc.
6 Skyline Drive
Hawthorne, NY 10532
Submission Date:
February 14, 1996

Review of a Waiver Request

The firm requests a waiver of the bioequivalence requirement for Fluocinonide Topical Solution USP, 0.05%, in accordance with 21 CFR 320.22 (b)(3) of the regulations. The ANDA was submitted on November 30, 1995. The agency issued refuse to file letter because the firm did not provide quantitative comparison of the formulation of their proposed drug product with that of the reference listed drug. The firm submitted the required information on February 14, 1996.

Fluocinonide is indicated for the relief of the inflammatory and pruritic manifestations of corticosteroid-responsive dermatoses. The reference listed drug is Lidex® (NDA #N18849) manufactured by Syntex Laboratories (Hamilton Pharma, CA).

FORMULATION: The firm provides following formulation based on quantitative analysis of test and reference products:

Ingredient	Test	Reference (Syntex)	Absolute Difference
Fluocinonide	.0524%*	.050%*	
Alcohol			
Citric Acid			
Di-isopropyl Adipate			
Propylene Glycol			
Water			

* quantity based on formula and was not determined through quantitative analysis

The firm has also provided the comparison of the physicochemical properties of test and reference products:

	Test	Reference
Appearance	Clear colorless solution, free from any particles	Clear colorless solution, free from any particles
pH	4.20	4.18
Specific Gravity	0.9499	0.9477

This reviewer compared the formula composition of the test product with that of reference product:

Not to be released under FOI

Ingredient	Test	Reference	Absolute difference
Fluocinonide	0.0524%	0.05%	
Alcohol			
Citric Acid			
Di-isopropyl Adipate			
Propylene Glycol			
Water			

* obtained by adding up other ingredients and subtracting from 100.

Comments:

1. The test product is a topical solution. The route of administration, dosage form, and active ingredient are the same as reference listed drug.

2. The inactive ingredients in the test product are qualitatively same as RLD. The difference in the concentrations of alcohol and di-isopropyl adipate between test and reference products are less than Propylene glycol concentration in test product is higher based on quantitative analysis and higher based on formula comparison than the reference product. The firm did not determine citric acid quantities. The concentration of citric acid is higher in test compared to reference based on formula comparison. However, the concentrations of all inactive ingredients in the test product are within the potency range given in the IIG for same route of administration.
The pH and specific gravity data provided by the firm show no significant differences between the two products.

3. As per interim guidance for inactive ingredients for topical solution, waiver can be granted if the test product is Q1 (qualitative) and Q2 (quantitative) same. The Q2 same meaning "essentially the same", i.e. within the +/-5% of the concentration of the RLD. If the test product is Q1 same, Q2 diff., then the ANDA is acceptable for filing with explanation as long as Q2 is not greater than maximum concentration in the IIG; may require *in vivo* BE study.

4. The test product comes under the category of Q1 same, Q2 diff. The concentrations of all inactive ingredients are less than the maximum concentration for topical solution in the IIG. However, according to interim guidance for inactive ingredients, some drugs in this category (Q1 same, Q2 diff) may require *in vivo* BE

study. The criteria as to which drug would require BE study are being developed.

5. All excipients in topical products are considered exception excipients as per interim guidance for inactive ingredients. The acceptable potency range for propylene glycol in a topical solution is 3% to 99.99% (IIG, 1996). The concentration of propylene glycol in the test product is more than the reference product based on quantitative analysis. However, propylene glycol is an exception excipient and its concentration from the formulation; by quantitative analysis) is within the IIG poency range. There is no qualitative difference in ingredients between test and reference product. The pH and specific gravity data provided by the firm show no significant differences between the two products. Therefore, waiver may be granted.

Recommendation:

The Division of Bioequivalence agrees that the information submitted by Taro Pharmaceuticals U.S.A. demonstrates that fluocinonide topical solution, USP 0.05% falls under 21 CFR 320.22 (b)(3) of the bioavailability/bioequivalence regulations. The waiver of the *in vivo* bioequivalence study requirements for the 0.05% topical solution of the test product is granted. From the bioequivalence point of view, the Division of Bioequivalence deems the test product to be bioequivalent to Lidex® topical solution 0.05% manufactured by Syntex.

Kuldeep R. Dhariwal, Ph.D.
Review Branch II
Division of Bioequivalence

RD INITIALED S.NERURKAR
FT INITIALED S.NERURKAR for 5/21/96 Date

Concur: Date 5/21/96
Keith Chan, Ph.D.
Director, Division of Bioequivalence

cc:ANDA #74799 (original), HFD-600 (Hare), HFD-630, HFD-655 (Nerurkar, Dhariwal), Drug File, Division File

Draft: 051796; Final: 052196